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VALIDATED RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF DEXRABEPRAZOLE AND DOMPERIDONE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

A rapid and precise reverse phase high performance liquid chromatographic method has been developed for the validated of Domperidone and Dexrabeprazole, in its pure form as well as in tablet dosage form. Chromatography was carried out on a Symmetry C18 (4.6 x 150mm, 5µm) column using a mixture of Methanol: Phosphate Buffer pH 3.5 (65:35) as the mobile phase at a flow rate of 1.0ml/min, the detection was carried out at 270 nm. The retention time of the Domperidone and Dexrabeprazole was 2.456, 4.312 ±0.02min respectively. The method produce linear responses in the concentration range of 5-25mg/ml of Domperidone and 2.5-12.5mg/ml of Dexrabeprazole. The method precision for the determination of assay was below 2.0%RSD. The method is useful in the quality control of bulk and pharmaceutical formulations.

Keywords: Domperidone, Dexrabeprazole, RP-HPLC, validation.

INTRODUCTION

Chemically it is Dexrabeprazole sodium (DEX) is R (+)-isomer of rabeprazole (2-[[[4-(3- methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl] 1H-benzimidazole). It is a proton pump inhibitor that suppresses gastric acid secretion. Domperidone (DOM) is 5-chloro-1- [1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)propyl]-piperidin-4-yl]-1,3-dihydro-2H-benzimi-dazol-2-one.

It is a dopamine receptor (D2) antagonist which is used as antiemetic drug and is official in British Pharmacopoeia. Domperidone alone or in combination with other drugs isreported to be estimated by HPLC, Spectrophotometry, HPTLC , LC-MS [1-5]. Whereas no analytical method is reported for analysis of dexrabeprazole [6-9]. The present work describes a method for determination of DEX and DOM in capsules using RP-HPLC The method is simple and requires less time for routine analysis. The proposed method was optimized & validated as per ICH [10-13] guidelines.

MATERIALS AND METHODS

Materials: Standard gift samples of DEX and DOM were provided by Sura Labs pvt Ltd, Hyderabad Combined dose capsule formulation R-Pure D (10 mg of DEX and 30mg of DOM, Manufactured by Emcure), were purchased from local market. All chemicals and reagents used were of HPLC grade.

Instrumentation

Lachrom HPLC quaternary gradient system (Make: Waters-2695) with L-7100 double reciprocating pump and Lab India UV detector was used. Chromatographic data was acquired using Empower-2 software. A reversed-phase Thermo C18 column (250 × 4.6 mm i.d., particle size 5 µm) was used for separation.

Chromatographic conditions

Thermo C18 column (4.6 mm i.d. × 250 mm) was used as stationary phase. Acetonitrile: 0.025M potassium dihydrogen orthophosphate buffer (pH adjusted to 5.1 with triethylamine) in the ratio of 30:70 % v/v was used as mobile phase and was filtered before use through 0.45 µ membrane filter. A constant flow of 1.0 ml/min was maintained throughout the analysis. Detection was carried out using UV detector at 284 nm.

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To ascertain the suitability of the proposed chromatographic conditions, system suitability tests were carried out and the results are shown in Table 1. Chromatogram of standard solution containing DEX and DOM is shown in Fig. 1.

Preparation of standard calibration curves (Linearity)

Standard stock solution of DEX and DOM were prepared by transferring 10 mg of DEX and 20 mg DOM in 100ml volumetric flask. Sufficient amount of mobile phase was added, sonicated and remaining volume was made up to the mark with mobile phase. Aliquots of standard stock solution were appropriately diluted with mobile phase to obtain concentration range of 5-25 µg/ml for DEX and 2.5-12.5µg/ml for DOM. The diluted standard solutions with varying concentration were injected (in triplicate) into the HPLC system separately and chromatographed under above mentioned chromatographic conditions. Chromatographic peaks were recorded at 284 nm using UV detector. The calibration curves of mean peak area versus concentration were plotted

Linearity Plot:

The plot of Concentration (x) versus the Average Peak Area (y) data of DRUG is a straight line.

Y = mx + c

Slope (m) = 38776

Intercept (c) = 15288

Correlation Coefficient (r) = 0.999

Linearity Plot

The plot of Concentration (x) versus the Average Peak Area (y) data of DRUG is a straight line.

Y = mx + c

Slope (m) = 57144

Intercept (c) = 2194

Correlation Coefficient (r) = 0.999

Validation Criteria: The response linearity is verified if the Correlation Coefficient is 0.99 or greater.

CONCLUSION: Correlation Coefficient (r) is 0.99, and the intercept is 2194. These values meet the validation criteria.

Precision:

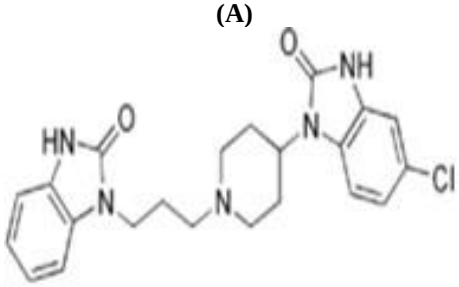
The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

Repeatability

Obtained Five (5) replicates of 100% accuracy solution as per experimental conditions. Recorded the peak areas and calculated % RSD.

Figure 1.Chemical structure of Domperidone (A) and Dexrabeprazole (B)

(A)



(B)

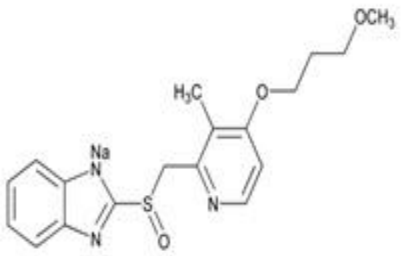


Figure 2. Chromatogram for linearity concentration-25 µg/ml of Domperidone& 12.5 µg/ml of Dexrabeprazole

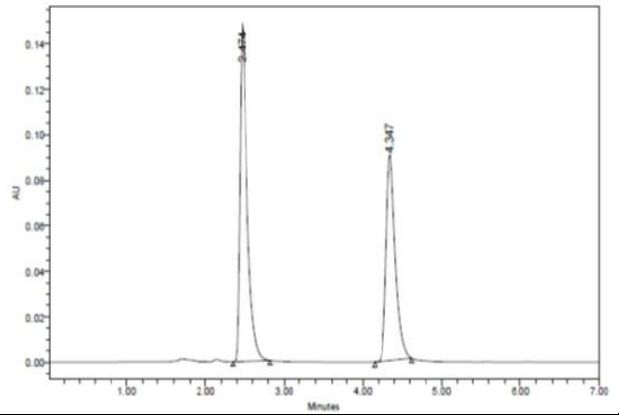


Figure 3. Calibration graph for Domperidone

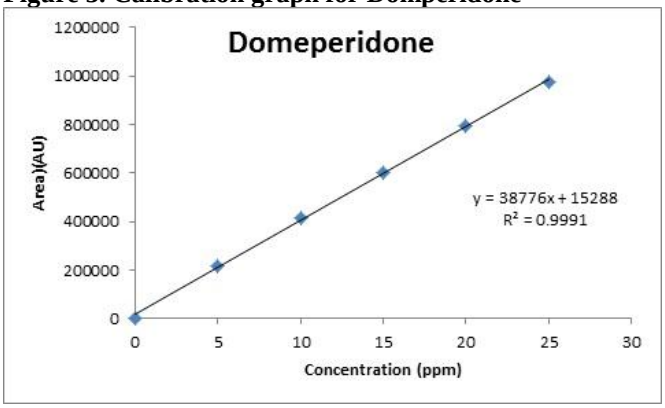


Figure 4. Calibration graph for Dexrabeprazole

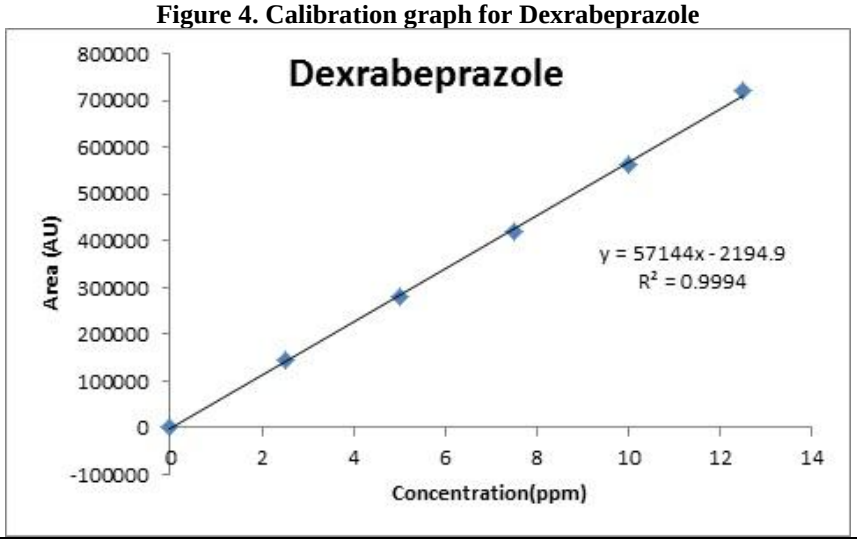


Table 1. Chromatographic Data For Linearity Study:

a. Domperidone:

Concentration Level (%)	Concentrationµg/ml	Average Peak Area
33.3	5	215760
66.6	10	417001
100	15	600435
133.3	20	791969
166.6	25	974736

b. **Dexrabeprazole**

Concentration Level (%)	Concentrationµg/ml	Average Peak Area
33	2.5	145474
66	5	279372
100	7.5	421045
133	10	562151
166	12.5	721671

Table 2. Results of repeatability for Domperidone

S. No.	Name	Rt	Area	Height	USP plate count	USP Tailing
1	Domperidone	2.453	603403	112688	5881.3	1.4
2	Domperidone	2.455	608107	113637	5844.1	1.3
3	Domperidone	2.453	607266	112849	5918.1	1.3
4	Domperidone	2.452	608776	112478	5847.3	1.4
5	Domperidone	2.450	609758	111779	5801.8	1.5
Mean			607462			
Std. Dev			2445.82			
% RSD			0.40			

Table 3. Results of method precession for Dexrabeprazole

S.No.	Name	Rt	Area	Height	USP plate count	USP Tailing	USP Resolution
1	Dexrabeprazole	4.289	429183	52411	5050.9	1.49	3.2
2	Dexrabeprazole	4.309	416643	52475	5084.8	1.5	3.2
3	Dexrabeprazole	4.306	424052	51841	5000.1	1.4	3.2
4	Dexrabeprazole	4.300	425235	51804	5026.4	1.51	3.2
5	Dexrabeprazole	4.295	416260	51274	5098.5	1.51	3.2

Mean			422274.6				
Std. Dev			5646.668				
% RSD			1.3				

Table 4. Results of Intermediate precision for Domperidone

S. No.	Name	Rt	Area	Height	USP plate count	USP Tailing
1	Domperidone	2.465	602386	111226	5075.9	1.5
2	Domperidone	2.472	608118	112497	5043.2	1.3
3	Domperidone	2.467	605566	110347	5029.9	1.5
4	Domperidone	2.466	608543	53992	5023.2	1.4
5	Domperidone	2.472	609288	55420	5061.3	1.4
6	Domperidone	3.424	607315	54154	5078.4	1.3
Mean			606869.3			
Std. Dev			2538.025			
% RSD			0.41			

Table 5. Results of Intermediate precision for Dexrabeprazole

S. No.	Name	Rt	Area	Height	USP plate count	USP Tailing	USP Resolution
1	Dexrabeprazole	4.323	422252	50991	5886.2	1.6	3.2
2	Dexrabeprazole	4.343	418090	50664	5947.5	1.5	3.2
3	Dexrabeprazole	4.324	424361	50295	5907.8	1.55	3.2
4	Dexrabeprazole	4.323	424692	49813	5890.0	1.50	3.2
5	Dexrabeprazole	4.342	411255	49826	5852.5	1.49	3.2
6	Dexrabeprazole	4.323	422252	50991	5756.8	1.50	3.2
Mean			420483.7				
Std. Dev			5096.974				
% RSD			1.2				

RESULTS AND DISCUSSION

The proposed chromatographic system was found suitable for effective separation and quantitation of DEX (RT-2.48 min) and DOM (RT-4.31 min) with good resolution, peak shapes and minimal tailing. The peak areas of the drugs were reproducible as indicated by low coefficient of variance indicating the repeatability of the proposed method.

Both the drugs were found to give linear detector response in the concentration range under study with correlation coefficient of 0.999 and 0.999 for DEX and DOM, respectively. The sample recoveries from the formulation were in good agreement with their respective label claim indicating that there is no interference from the capsule excipients. The method exhibited good selectivity and sensitivity. Percent recoveries for DEX and DOM were 99.38 % and 100.54 %, respectively indicating accuracy of the proposed method. %RSD for capsule analysis, recovery studies and intra-day & inter-day precision studies is less than 2. LOD and LOQ were found to be 0.1368 &0.4144 for DEX and 0.3378 & 1.0237 for DOM, respectively.

The results of robustness study also indicated that the method is robust and is unaffected by small deliberate variations in the method parameters.

SUMMARY

The analytical method was developed by studying different parameters. First of all, maximum absorbance was found to be at 270 nm and the peak purity was excellent. Injection volume was selected to be 10µl which gave a good peak area. The column used for study was Symmetry C_{18} because it was giving good peak.

Ambient temperature was found to be suitable for the nature of drug solution. The flow rate was fixed at 1.0ml/min because of good peak area and satisfactory retention time. Mobile phase is Methanol: Phosphate Buffer pH 3.5 (65:35) was fixed due to good symmetrical peak. So this mobile phase was used for the proposed study. Run time was selected to be 5 min because analyze gave peak around 2.456, 4.312 ±0.02min respectively and also to reduce the total run time. The percent recovery was found to be 98.0-102 was linear and precise over the same range. Both system and method precision was found to be accurate and well within range. The analytical method was found linearity over the range 5-25mg/ml of Domeperidone and 2.5-12.5 mg/ml of Dexrabeprazole of the target concentration. The analytical passed both robustness and ruggedness tests. On both cases, relative standard deviation was well satisfactory.

CONCLUSION

In the present investigation, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Domperidone and Dexrabeprazole in bulk drug and pharmaceutical dosage forms. This method was simple, since diluted samples are directly used without any preliminary chemical derivatisation or purification steps. Domperidone and Dexrabeprazolewas freely soluble in ethanol, methanol and sparingly soluble in water. Methanol: Phosphate Buffer pH 3.5 (65:35) was chosen as the mobile phase. The solvent system used in this method was economical. The %RSD values were within 2 and the method was found to be precise. The results expressed in Tables for RP-HPLC method was promising. The RP-HPLC method is more sensitive, accurate and precise compared to the Spectrophotometric methods. This method can be used for the routine determination of Domperidone and Dexrabeprazolein bulk drug and in Pharmaceutical dosage forms.

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CONFLICT OF INTEREST: NIL

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